Exostosis induced by somatropin therapy in paediatric patients: an unknown, but predictable, adverse reaction.

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Growth hormone (GH) has an important homeostatic role, acting on the metabolism of muscle, adipose tissue, several vital organs (i.e. pancreas, kidneys). It also coordinates articular and bone cartilage linear growth during adolescence.
Growth hormone deficiency (GHD) due to genetic, acquired or idiopathic mechanisms is thus a relevant clinical condition. Drugs containing GH are licensed for the treatment of GHD and are generally well tolerated with minimal adverse effects limited to local skin reactions, edema, paresthesia, muscle and joint pain. GH treatment is widely used also in children with severe orthopaedic complications as slipped capital femoral epiphysis, Legg-Calvé-Perthes disease, scoliosis and carpal tunnel syndrome even if not in a GHD condition.
Herein we report on an adverse drug reaction (ADRs) due to exogenous GH treatment that occurred in two paediatric patients (a male and a female) affected by growth hormone deficiency. Following GH administration at therapeutic doses the two children developed exostosis, a cartilage-forming tumor occurring most commonly in the metaphyses of long bones. The inability to discontinue therapy with GH resulted in an objective worsening of the symptoms of the patient.
The mechanism of action through which GH had induced this ADR is likely to be the same responsbile for its pharmacological activity. GH influences chondrocyte proliferation by the interaction with the receptors of chondrocytes inducing the activation of the cytoplasmic kinase JAK-2, which phosphorylates and activates transcription factors regulating the expression of the chondrocyte genes.
Whereas the mechanism of action of GH indcuing the ADR appeatrs to be the same responsible for its therapeutic action of the hormone, it is surprising that such ADR was not reported previously. Whether uncommon concomitant factors are relevant to the development of exostosis needs to be elucidated.

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